10/816,544

UPDATED: 4 May 2008 (20080504/ED)

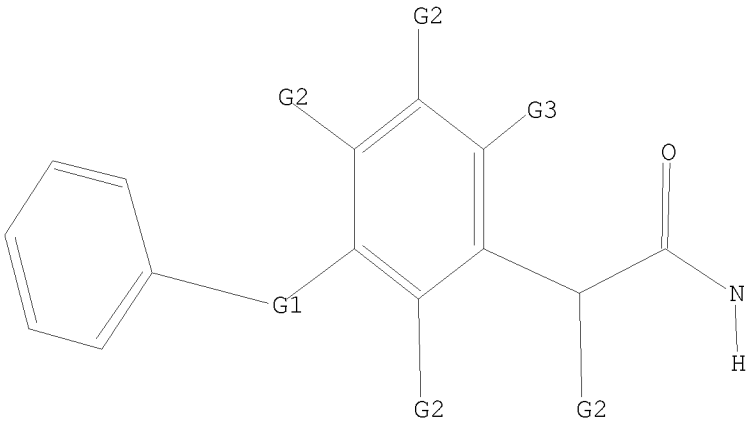
Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=>
Uploading C:\Program Files\Stnexp\Queries\10816544c.str

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 NH,O

G2 X,OH,H

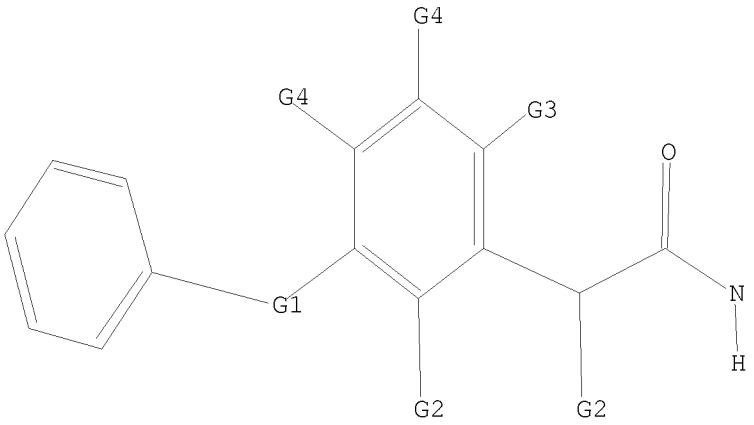
G3 CN,Ak

Structure attributes must be viewed using STN Express query preparation.

=>
Uploading C:\Program Files\Stnexp\Queries\10816544d.str

L2 STRUCTURE UPLOADED

=> d
L2 HAS NO ANSWERS
L2 STR



G1 NH,O

G2 X,OH,H

G3 CN,Ak

G4 OH,C,X,H

Structure attributes must be viewed using STN Express query preparation.

=> s l2 full
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 17:59:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 3783 TO ITERATE

100.0% PROCESSED 3783 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

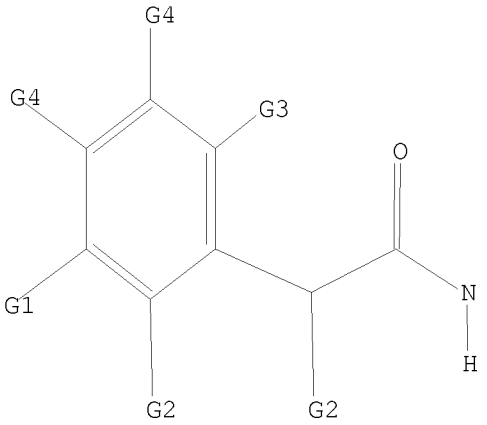
L3 0 SEA SSS FUL L2

L4 0 L3

=>
Uploading C:\Program Files\Stnexp\Queries\10816544e.str

L5 STRUCTURE UPLOADED

=> d
L5 HAS NO ANSWERS
L5 STR



G1 NH,O

G2 X,OH,H

G3 CN,Ak

G4 OH,C,X,H

Structure attributes must be viewed using STN Express query preparation.

=> s l5 full
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 18:00:29 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 59709 TO ITERATE

100.0% PROCESSED 59709 ITERATIONS 117 ANSWERS
SEARCH TIME: 00.00.01

L6 117 SEA SSS FUL L5

L7 16 L6

=> s l7 and pyridine
223941 PYRIDINE
L8 3 L7 AND PYRIDINE

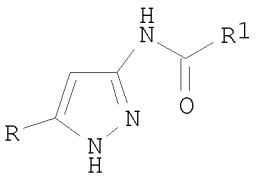
=> s l7 and py<2003
22929897 PY<2003
L9 11 L7 AND PY<2003

=> d 1-11 ibib abs hitstr

L9 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:374223 CAPLUS
DOCUMENT NUMBER: 144:412501
TITLE: Preparation of 3(5)-acylaminopyrazole derivatives for use as therapeutic agents, particularly antitumor agents
INVENTOR(S): Pevarello, Paolo; Orsini, Paolo; Traquandi, Gabriella; Varasi, Mario; Fritzen, Edward L.; Warpehoski, Martha A.; Pierce, Betsy S.; Brasca, Maria Grabriella
PATENT ASSIGNEE(S): Pharmacia Italia S.p.A., Italy; Pharmacia & Upjohn Company LLC
SOURCE: U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 372,831, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7034049	B1	20060425	US 2002-48486	20020501
WO 2001012189	A1	20010222	WO 2000-US6699	20000505 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6218418	B1	20010417	US 2000-667603	20000922 <--
PRIORITY APPLN. INFO.:			US 1999-372831	B2 19990812
			WO 2000-US6699	W 20000505
			US 2000-560400	A1 20000428

OTHER SOURCE(S): MARPAT 144:412501
GI



I

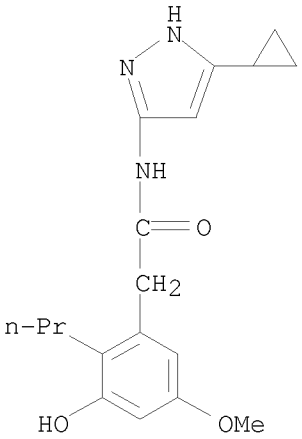
AB Compds. (e.g., N-(5-cyclopropyl-1H-pyrazol-3-yl)-2,2-diphenylacetamide) which are 3-amino-pyrazole derivs. represented by formula I (wherein R = C3-C6 cycloalkyl group optionally substituted by a straight or branched C1-C6 alkyl or arylalkyl group; R1 = a straight or branched C1-C6 alkyl, C2-C4 alkenyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, arylalkyl, arylcarbonyl, aryloxyalkyl or arylalkenyl group, each of which may be optionally further substituted) are claimed. A process for preparing the

3-aminopyrazole derivs. comprises: (a) reacting RCO2R2 (R2 = alkyl), with MeCN in the presence of a basic agent, to obtain RC(O)CH2CN; (b) reacting RC(O)CH2CN with hydrazine hydrate to obtain an 3-amino-5-R-1H-pyrazole; (c) oxidizing the 3-amino-5-R-1H-pyrazole to obtain the nitro analog; (d) reacting the nitro compound with tert-butoxycarbonyl anhydride (Boc2O) to obtain the N-Boc derivative which was reduced; (e) reacting this amino compound with R1C(O)X (X = OH or a suitable leaving group) to obtain the N1-Boc-protected I; and (g) hydrolyzing this intermediate in an acidic medium to obtain I. The compds. are useful for the treatment of cancer, cell proliferative disorders, Alzheimer's disease, viral infections, auto-immune diseases or neurodegenerative diseases (no data is given). Pharmaceutical compns. containing I are also claimed.

IT 326825-31-4P, N-(5-Cyclopropyl-1H-pyrazol-3-yl)-2-(5-methoxy-3-hydroxy-2-propylphenyl)acetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3(5)-acylaminopyrazole derivs. for use as therapeutic agents, particularly antitumor agents)

RN 326825-31-4 CAPLUS

CN Benzeneacetamide, N-(5-cyclopropyl-1H-pyrazol-3-yl)-3-hydroxy-5-methoxy-2-propyl- (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:275956 CAPLUS
DOCUMENT NUMBER: 136:294655
TITLE: Aminopyridinyl-, aminoguanidinyl- and alkoxyguanidinyl- substituted phenyl acetamides as protease inhibitors
INVENTOR(S): Pan, Wenxi; Lu, Tianbao; Markotan, Thomas P.; Tomczuk, Bruce E.
PATENT ASSIGNEE(S): 3-Dimensional Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028825	A2	20020411	WO 2001-US31249	20011005 <--
WO 2002028825	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2423883	A1	20020411	CA 2001-2423883	20011005 <--
AU 2002011464	A	20020415	AU 2002-11464	20011005 <--
US 20020061872	A1	20020523	US 2001-971000	20011005 <--
US 6521663	B2	20030218		
EP 1324981	A2	20030709	EP 2001-979513	20011005
EP 1324981	B1	20060823		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003003149	A2	20040128	HU 2003-3149	20011005
BR 2001014263	A	20040302	BR 2001-14263	20011005
JP 2004510759	T	20040408	JP 2002-532411	20011005
ZA 2003003091	A	20040722	ZA 2003-3091	20011005
NZ 525438	A	20040924	NZ 2001-525438	20011005
CN 1568307	A	20050119	CN 2001-818254	20011005
AT 337299	T	20060915	AT 2001-979513	20011005
ES 2269474	T3	20070401	ES 2001-979513	20011005
US 20030073833	A1	20030417	US 2002-262871	20021003
US 6900231	B2	20050531		
NO 2003001390	A	20030603	NO 2003-1390	20030326
MX 2003PA02998	A	20040212	MX 2003-PA2998	20030404
IN 2003KN00504	A	20050311	IN 2003-KN504	20030423
HK 1058032	A1	20070316	HK 2004-100042	20040102
US 20050159457	A1	20050721	US 2005-32297	20050110

PRIORITY APPLN. INFO.:	US 2000-238132P	P	20001006
	US 2001-971000	A3	20011005
	WO 2001-US31249	W	20011005
	US 2002-262871	A1	20021003

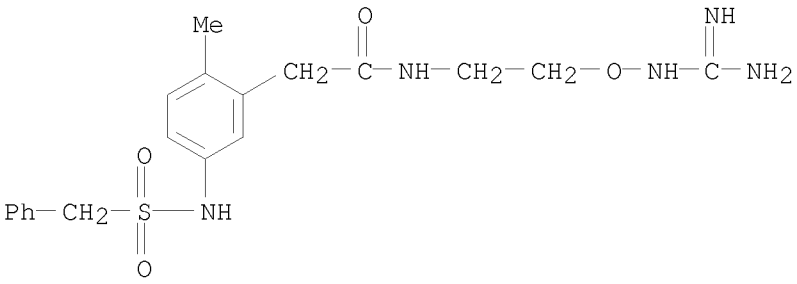
OTHER SOURCE(S): MARPAT 136:294655

AB The compds. of the invention are potent inhibitors of proteases, especially trypsin-like serine proteases, such as thrombin and factor Xa. Compns. for inhibiting loss of blood platelets, inhibiting formation of blood platelet aggregates, inhibiting formation of fibrin, inhibiting thrombus formation, and inhibiting embolus formation are described. Other uses of compds. of the invention are as anticoagulants either embedded in or phys. linked to materials used in the manufacture of devices used in blood collection, blood circulation, and blood storage, such as catheters, blood dialysis machines, blood collection syringes and tubes, blood lines and stents. Addnl., the compds. can be detectably labeled and employed for in vivo imaging for thrombi. The 11 title compds. prepared have Ki values for

human thrombin of between 0.0028 and 20μM. Among the 11 title compds. prepared by standard methods were 98% N-[2-(amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-phenylethyl)amino]-6-chloro-2-fluorophenyl}acetamide, 99% N-[2-(amidinoaminooxy)ethyl]-2-{3-[2,2-difluoro-2-(4-fluoronaphthyl)ethylamino]-6-chloro-2-fluorophenyl}acetamide and 100% N-[2-(guanidinooxy)ethyl]-2-[2-chloro-5-(benzylsulfonylamino)phenyl]acetamide.

IT 409081-63-6P 409081-64-7P 409081-65-8P
409081-66-9P 409081-67-0P 409082-40-2P
409082-41-3P 409082-42-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of aminopyridinyl-, aminoguanidinyl- and alkoxyguanidinyl-substituted phenylacetamides as anticoagulants)

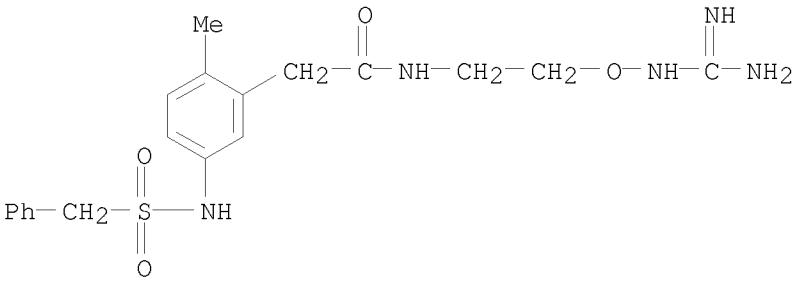
RN 409081-63-6 CAPLUS
CN Benzeneacetamide, N-[2-[[(aminoiminomethyl)amino]oxy]ethyl]-2-methyl-5-[[(phenylmethyl)sulfonyl]amino]- (CA INDEX NAME)



RN 409081-64-7 CAPLUS
CN Benzeneacetamide, N-[2-[[(aminoiminomethyl)amino]oxy]ethyl]-2-methyl-5-[[(phenylmethyl)sulfonyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

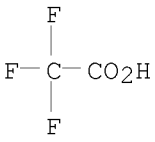
CM 1

CRN 409081-63-6
CMF C19 H25 N5 O4 S

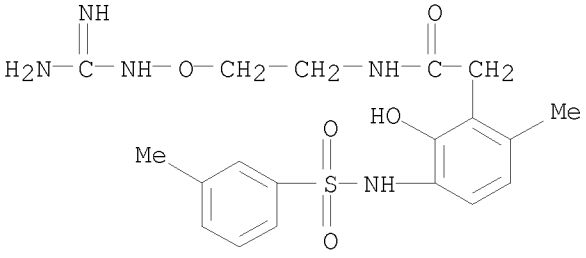


CM 2

CRN 76-05-1
CMF C2 H F3 O2

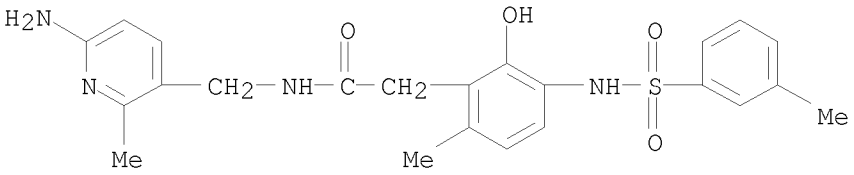


RN 409081-65-8 CAPLUS
CN Benzeneacetamide, N-[2-[[(aminoiminomethyl)amino]oxy]ethyl]-2-hydroxy-6-methyl-3-[[(3-methylphenyl)sulfonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



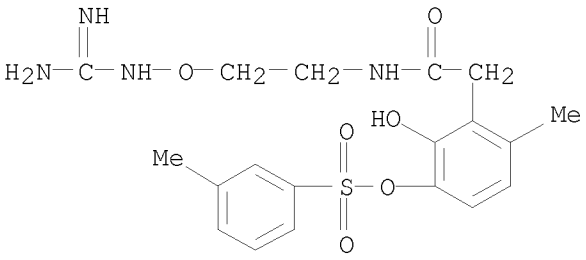
● HCl

RN 409081-66-9 CAPLUS
CN Benzeneacetamide, N-[(6-amino-2-methyl-3-pyridinyl)methyl]-2-hydroxy-6-methyl-3-[[(3-methylphenyl)sulfonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



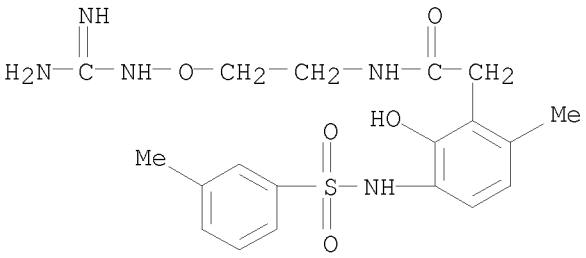
● HCl

RN 409081-67-0 CAPLUS
CN Benzenesulfonic acid, 3-methyl-, 3-[2-[[2-[[(aminoiminomethyl)amino]oxy]ethyl]amino]-2-oxoethyl]-2-hydroxy-4-methylphenyl ester, monohydrochloride (9CI) (CA INDEX NAME)

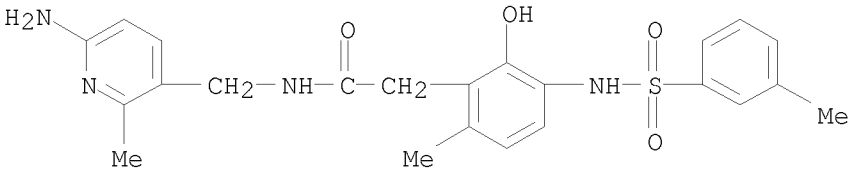


● HCl

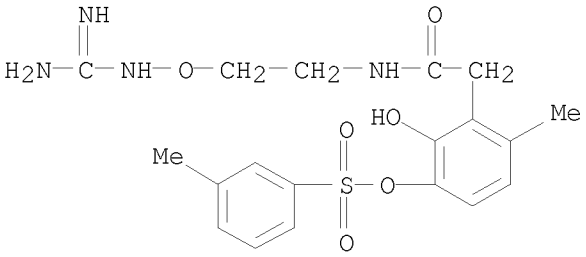
RN 409082-40-2 CAPLUS
CN Benzeneacetamide, N-[2-[[(aminoiminomethyl)amino]oxy]ethyl]-2-hydroxy-6-methyl-3-[[(3-methylphenyl)sulfonyl]amino]- (CA INDEX NAME)



RN 409082-41-3 CAPLUS
CN Benzeneacetamide, N-[(6-amino-2-methyl-3-pyridinyl)methyl]-2-hydroxy-6-methyl-3-[[(3-methylphenyl)sulfonyl]amino]- (CA INDEX NAME)

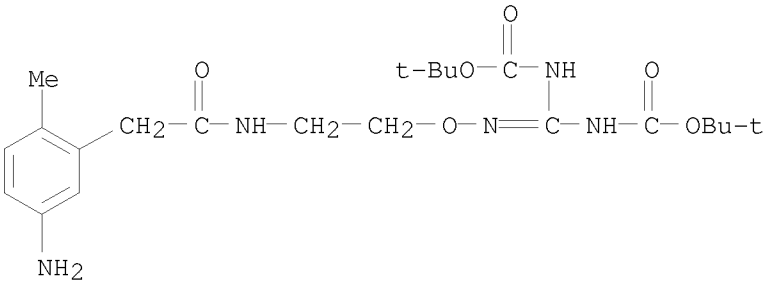


RN 409082-42-4 CAPLUS
CN Benzenesulfonic acid, 3-methyl-, 3-[2-[[2-[[(aminoiminomethyl)amino]oxy]ethyl]amino]-2-oxoethyl]-2-hydroxy-4-methylphenyl ester (CA INDEX NAME)

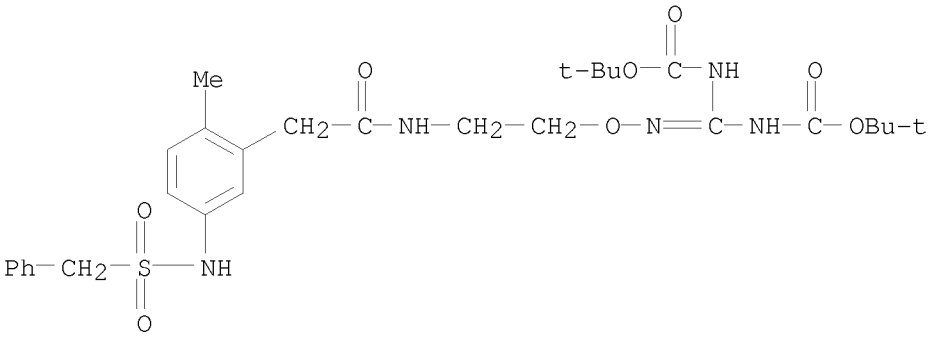


IT 409082-17-3P 409082-19-5P 409082-26-4P
409082-36-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminopyridinyl-, aminoguanidinyl- and alkoxyguanidinyl-substituted phenylacetamides as anticoagulants)

RN 409082-17-3 CAPLUS
CN 5-Oxa-2,4,8-triazadec-2-enoic acid, 10-(5-amino-2-methylphenyl)-3-[[(1,1-dimethylethoxy)carbonyl]amino]-9-oxo-, 1,1-dimethylethyl ester (CA INDEX NAME)

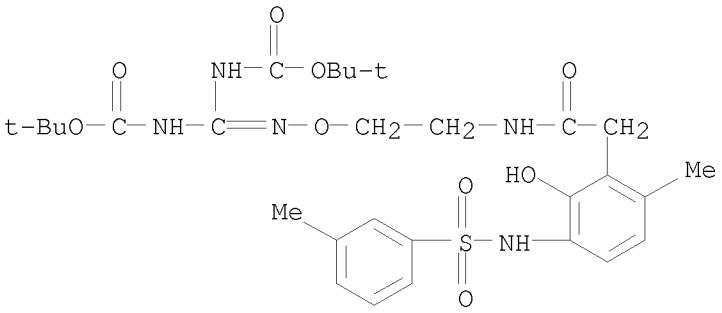


RN 409082-19-5 CAPLUS
CN 5-Oxa-2,4,8-triazadec-2-enoic acid, 3-[[(1,1-dimethylethoxy)carbonyl]amino]-10-[2-methyl-5-[[(phenylmethyl)sulfonyl]amino]phenyl]-9-oxo-, 1,1-dimethylethyl ester (CA INDEX NAME)

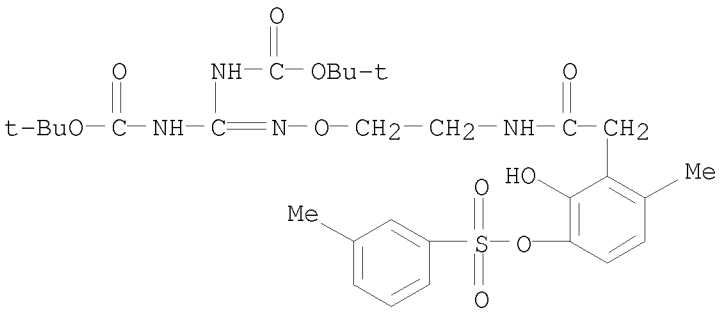


RN 409082-26-4 CAPLUS

CN 5-Oxa-2,4,8-triazadec-2-enoic acid, 3-[[(1,1-dimethylethoxy)carbonyl]amino]-10-[2-hydroxy-6-methyl-3-[[(3-methylphenyl)sulfonyl]amino]phenyl]-9-oxo- , 1,1-dimethylethyl ester (CA INDEX NAME)



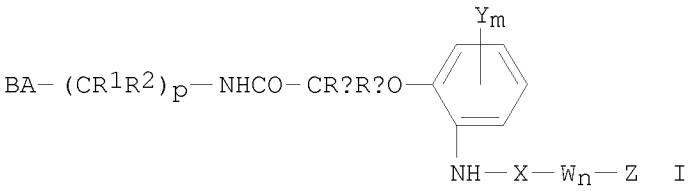
RN 409082-36-6 CAPLUS
CN 5-Oxa-2,4,8-triazadec-2-enoic acid, 3-[[(1,1-dimethylethoxy)carbonyl]amino]-10-[2-hydroxy-6-methyl-3-[[(3-methylphenyl)sulfonyl]oxy]phenyl]-9-oxo-, 1,1-dimethylethyl ester (CA INDEX NAME)



L9 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:719012 CAPLUS
DOCUMENT NUMBER: 135:280431
TITLE: Photographic element and compound and process useful therewith
INVENTOR(S): Romanet, Robert F.; Vreeland, William B.; Harder, John W.; Brown, Christopher T.; Conley, Scott R.; Youngblood, Michael P.
PATENT ASSIGNEE(S): Eastman Kodak Company, USA
SOURCE: U.S., 52 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6296997 B1 20011002 US 2000-707586 20001107 <--
EP 1205796 A2 20020515 EP 2001-204126 20011029 <--
EP 1205796 A3 20021211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2002162718 A 20020607 JP 2001-342355 20011107 <--
PRIORITY APPLN. INFO.: US 2000-707586 A 20001107
OTHER SOURCE(S): MARPAT 135:280431
GI



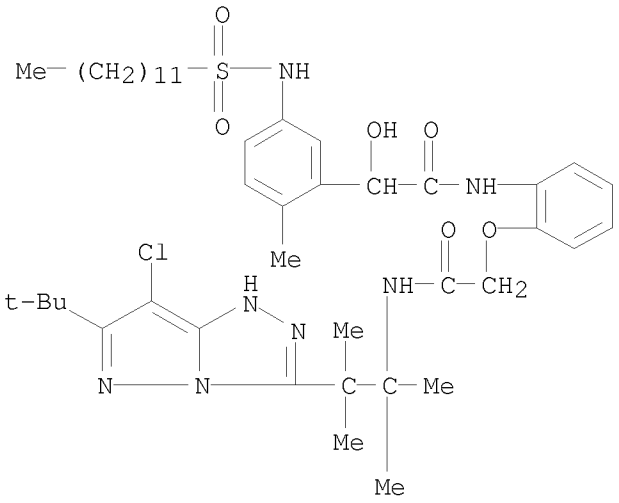
I

AB The invention describes a silver halide photog. element containing a dye-forming bicyclic azole coupler having a phenoxy substituent containing an ortho substituent for better color rendition. The photog. element comprises a light-sensitive Ag halide emulsion layer having associated therewith a bicyclic azole dye-forming coupler compound (I) where BA = a bicyclic azole coupler nucleus with -(C(R1)(R2))P- bonded to a ring C in a non-coupling position of the coupler nucleus; p is 1 or 2, and each R1 and R2 is independently selected from H and a substituent group, provided that any 2 of R1 and R2 may join to form a ring; Ra and Rb are each independently selected from H and a substituent group, provided that substituent groups may join to form a ring; each Y is an independently selected substituent and m is 0-4; X is selected from the group consisting of -C(O)-, -S(O)2-, -S(O)-, and -P(O)(OH)-; W is a connecting group having a chain of up to 4 atoms between X and Z, and n = 0 or 1; and(a) when n = 0, Z is -NHR5 where R5 is H or a substituent, and (b) when n = 1, Z is selected from -OH, -SO2NHR5, and -NHR6 where R5 is H or a substituent group and R6 is a substituent bonded to -NH- by an electron withdrawing group in R6; provided that the ClogP value of the coupler compound is at least 5.0. The element provides improved color rendition.

IT 363595-70-4
RL: NUU (Other use, unclassified); TEM (Technical or engineered material use); USES (Uses)
(photog. element containing dye-forming bicyclic azo coupler for better color reproduction)

RN 363595-70-4 CAPLUS

CN Benzeneacetamide, N-[2-[2-[[2-[7-chloro-6-(1,1-dimethylethyl)-1H-pyrazolo[5,1-c]-1,2,4-triazol-3-yl]-1,1,2-trimethylpropyl]amino]-2-oxoethoxy]phenyl]-5-[(dodecylsulfonyl)amino]-α-hydroxy-2-methyl- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

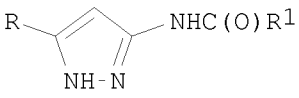
L9 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:137023 CAPLUS
DOCUMENT NUMBER: 134:178552
TITLE: 3(5)-Acylaminopyrazole derivatives, process for their preparation and their use as antitumor agents
INVENTOR(S): Pevarello, Paolo; Orsini, Paolo; Traquandi, Gabriella; Varasi, Mario; Fritzen, Edward L.; Warpehoski, Martha A.; Pierce, Betsy S.; Brasca, Maria Grabriella
PATENT ASSIGNEE(S): Pharmacia & Upjohn S.p.A., Italy; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012189	A1	20010222	WO 2000-US6699	20000505 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2383555	A1	20010222	CA 2000-2383555	20000505 <--
AU 2000049714	A	20010313	AU 2000-49714	20000505 <--
EP 1202733	A1	20020508	EP 2000-931906	20000505 <--
EP 1202733	B1	20051005		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL						
BR 2000013143	A	20020611	BR 2000-13143		20000505	<--
JP 2003507329	T	20030225	JP 2001-516535		20000505	
EE 200200065	A	20030415	EE 2002-65		20000505	
HU 2002003542	A2	20030528	HU 2002-3542		20000505	
HU 2002003542	A3	20030728				
NZ 517237	A	20040227	NZ 2000-517237		20000505	
AT 305782	T	20051015	AT 2000-931906		20000505	
ES 2249270	T3	20060401	ES 2000-931906		20000505	
US 6218418	B1	20010417	US 2000-667603		20000922	<--
NO 2002000684	A	20020403	NO 2002-684		20020211	<--
HR 2002000128	A1	20030430	HR 2002-128		20020212	
MX 2002PA01498	A	20030721	MX 2002-PA1498		20020212	
ZA 2002001511	A	20030311	ZA 2002-1511		20020222	
BG 106480	A	20020930	BG 2002-106480		20020305	<--
US 7034049	B1	20060425	US 2002-48486		20020501	
PRIORITY APPLN. INFO.:			US 1999-372831	A	19990812	
			US 2000-560400	A1	20000428	
			WO 2000-US6699	W	20000505	

OTHER SOURCE(S): MARPAT 134:178552

GI



I

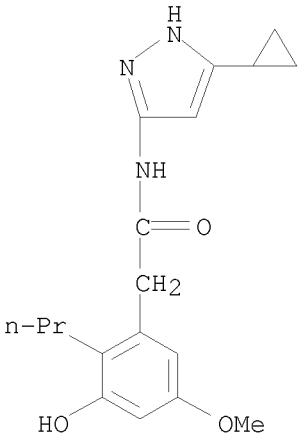
AB Compds. which are 3-acylaminopyrazole derivs. (I; e.g. N-(5-cyclopropyl-1H-pyrazol-3-yl)-2,2-diphenylacetamide) wherein R is C3-C6 cycloalkyl group optionally substituted by a straight or branched C1-C6 alkyl or arylalkyl group; R1 is a straight or branched C1-C6 alkyl, C2-C4 alkenyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, arylalkyl, arylcarbonyl, aryloxyalkyl or arylalkenyl group, each of which may be optionally further substituted as indicated in the description; or a pharmaceutically acceptable salt thereof, processes for their preparation and their therapeutic uses. The compds. are useful for the treatment of cancer, cell proliferative disorders, Alzheimer's disease, viral infections, auto-immune diseases or neurodegenerative diseases, but no quant. test results are presented. The cancer is selected from carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratoacanthoma, thyroid follicular cancer and Kaposi's sarcoma. The cell proliferative disorder is selected from benign prostate hyperplasia, familial adenomatosis polyposis, neuro-fibromatosis, psoriasis, vascular smooth cell proliferation associated with atherosclerosis, pulmonary fibrosis, arthritis glomerulonephritis and post-surgical stenosis and restenosis. The method of treatment provides tumor angiogenesis and metastasis inhibition, cell cycle inhibition or cdk/cyclin dependent inhibition, and treatment or prevention of radiotherapy-induced or chemotherapy-induced alopecia. A process for preparing the 3-aminopyrazole derivative or the pharmaceutically acceptable salt thereof, comprising: (a) reacting RCO2R2 (R2 = alkyl), with MeCN in the

presence of a basic agent, to obtain RC(O)CH2CN; (b) reacting RC(O)CH2CN with hydrazine hydrate to obtain an 3-amino-5-R-1H-pyrazole; (c) oxidizing the 3-amino-5-R-1H-pyrazole to obtain the nitro analog; (d) reacting the nitro compound with tert-butoxycarbonyl anhydride (Boc2O) to obtain the N-Boc derivative; (e) reducing this BOC derivative to obtain the amino analog; (f) reacting this amino compound with R1C(O)X (X = OH or a suitable leaving group) to obtain the N1-Boc-protected I; and (g) hydrolyzing this intermediate in an acidic medium to obtain I. Other methods of preparation are also claimed.

IT 326825-31-4P, N-(5-Cyclopropyl-1H-pyrazol-3-yl)-2-(5-methoxy-3-hydroxy-2-propylphenyl)acetamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(acylaminopyrazole derivs., process for preparation and use as antitumor agents)

RN 326825-31-4 CAPLUS

CN Benzeneacetamide, N-(5-cyclopropyl-1H-pyrazol-3-yl)-3-hydroxy-5-methoxy-2-propyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:307678 CAPLUS

DOCUMENT NUMBER: 133:150300

TITLE: Leaving group effects in reductively triggered fragmentation of 4-nitrobenzyl carbamates

AUTHOR(S): Sykes, Bridget M.; Hay, Michael P.; Bohinc-Herceg, Dubravka; Helsby, Nuala A.; O'Connor, Charmian J.; Denny, William A.

CORPORATE SOURCE: Faculty of Medical and Health Sciences, Auckland Cancer Society Research Centre, The University of Auckland, Auckland, N. Z.

SOURCE: Perkin 1 (2000), (10), 1601-1608
CODEN: PERKF9; ISSN: 1470-4358

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal
LANGUAGE: English
GI

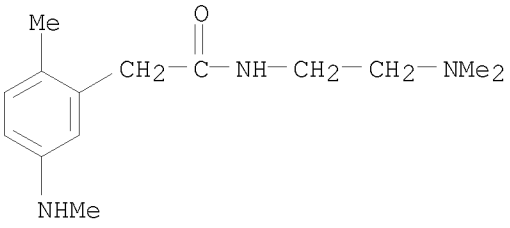
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The rates and extent of release of a series of substituted anilines from 4-nitrobenzyl carbamates, following nitro group reduction by radiolytic, enzymic and chemical methods, are reported. The yield of released anilines decreased over the pH range 4-7, but was independent of the basicity of the leaving aniline. Detailed studies of the fragmentation of one example identified the 4-hydroxylamine as the key intermediate. At pH greater than 5 the released aniline I condenses with a reactive 4-iminoquinomethane intermediate to give amine II, thus depleting the measurable amount of aniline I released. At pH less than 5 the release of amine proceeds to completion. The efficiency of reductively triggered release of anilines (III; R=H,Me,OMe,SO2Me) varied with small changes in the leaving group, but this was not uniformly related to aniline basicity. The competing reaction of the released aniline I to form amine II lowers the efficiency of release of I. This reaction occurs at the relatively high concns. (50 μM) used in the study and indicates the released effector amine should be toxic at concns. considerably lower than 50 μM. This highlights the need for prodrugs of very potent cytotoxic effectors to be used in tumor-directed nitroreductase enzyme-prodrug therapy.

IT 287120-22-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(leaving group effects in reductively triggered fragmentation of 4-nitrobenzyl carbamates)

RN 287120-22-3 CAPLUS

CN Benzeneacetamide, N-[2-(dimethylamino)ethyl]-2-methyl-5-(methylamino)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

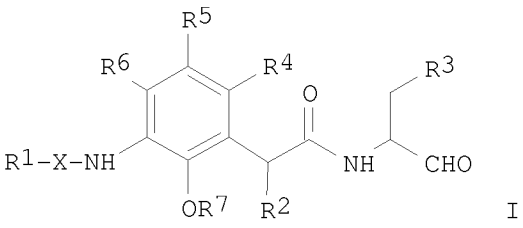
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:354477 CAPLUS

DOCUMENT NUMBER: 130:352556
TITLE: Synthesis of substituted 3-amino-2-hydroxyphenylacetamide derivatives as enzyme inhibitors
INVENTOR(S): Semple, Joseph Edward; Lim-Wilby, Marguerita S.; Brunck, Terence K.
PATENT ASSIGNEE(S): Corvas International, Inc., USA
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926920	A1	19990603	WO 1998-US25167	19981123 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6011047	A	20000104	US 1997-980114	19971126 <--
US 6204384	B1	20010320	US 1997-979440	19971126 <--
AU 9916056	A	19990615	AU 1999-16056	19981123 <--
PRIORITY APPLN. INFO.:			US 1997-979440 A	19971126
			US 1997-980114 A	19971126
			WO 1998-US25167 W	19981123

OTHER SOURCE(S): MARPAT 130:352556
GI



I

AB Peptide aldehydes I [X = SO2, NR'SO2, CO, OCO, NHCO, P(O)R'', or direct link (R' = H, alkyl, aryl, aralkyl; R'' = NHR', OR', R', SR'); R1 = (un)substituted alkyl, cycloalkylalkyl, cycloalkyl, heterocycloalkyl, aryl, etc.; R2 = H, alkyl, alkenyl; R3 = HN:C(NH2)NH(CH2)d (d = 0-5), 3- or 4-guanylcyclohexyl, 1-guanyl-3- or -4-piperidinyl; m- or p-guanylphenyl; R4, R5, R6 = R1, OR1, NHR1, SR1, S(O)R1, CF3, CF2H, OCF3, OCF2H, halo, etc.; R7 = R1, CF3, CF2H, etc.] were prepared as enzyme inhibitors. Thus, N-[[2-hydroxy-3-(benzylsulfonylamino)-6-

methylphenyl]acetyl]-L-argininal (in cyclol form) trifluoroacetate was prepared and showed IC50 = 3.19 nM for inhibition of thrombin.

IT 225096-31-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of substituted aminohydroxyphenylacetamide derivs. as enzyme inhibitors)

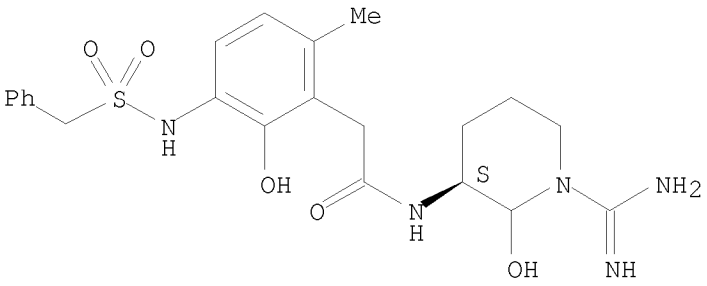
RN 225096-31-1 CAPLUS

CN Benzeneacetamide, N-[(3S)-1-(aminoiminomethyl)-2-hydroxy-3-piperidinyl]-2-hydroxy-6-methyl-3-[[(phenylmethyl)sulfonyl]amino]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

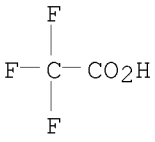
CRN 225096-30-0
CMF C22 H29 N5 O5 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT 225096-29-7P 225096-41-3P 225096-46-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of substituted aminohydroxyphenylacetamide derivs. as enzyme inhibitors)

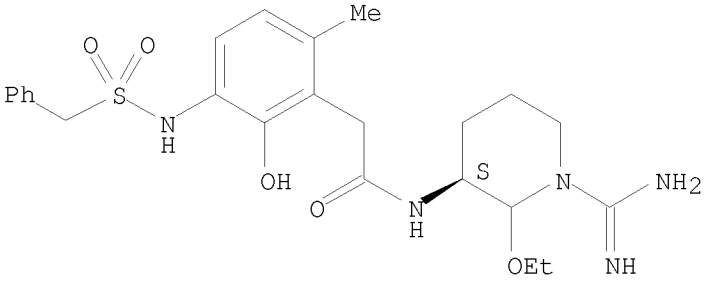
RN 225096-29-7 CAPLUS

CN Benzeneacetamide, N-[(3S)-1-(aminoiminomethyl)-2-ethoxy-3-piperidinyl]-2-hydroxy-6-methyl-3-[[(phenylmethyl)sulfonyl]amino]-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

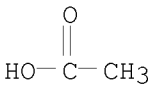
CRN 225096-28-6
CMF C24 H33 N5 O5 S

Absolute stereochemistry.



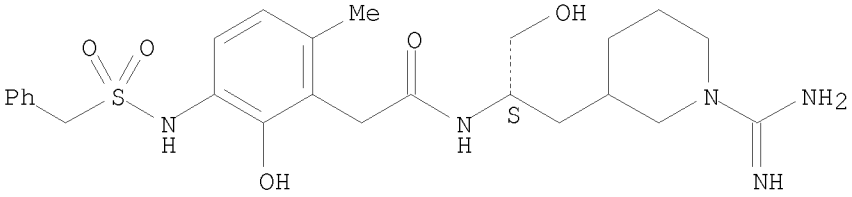
CM 2

CRN 64-19-7
CMF C2 H4 O2

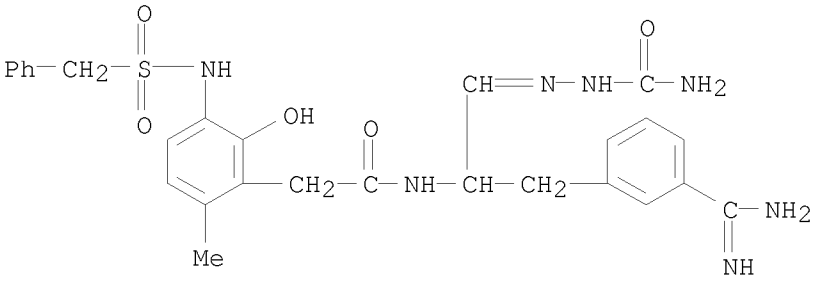


RN 225096-41-3 CAPLUS
CN Benzeneacetamide, N-[(1S)-2-[1-(aminoiminomethyl)-3-piperidinyl]-1-(hydroxymethyl)ethyl]-2-hydroxy-6-methyl-3-[[(phenylmethyl)sulfonyl]amino]- (CA INDEX NAME)

Absolute stereochemistry.



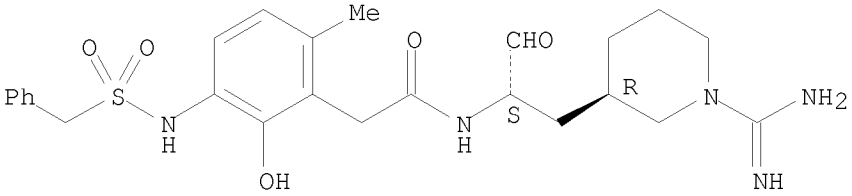
RN 225096-46-8 CAPLUS
CN Hydrazinecarboxamide, 2-[3-[3-(aminoiminomethyl)phenyl]-2-[[[2-hydroxy-6-methyl-3-[[(phenylmethyl)sulfonyl]amino]phenyl]acetyl]amino]propylidene]- (9CI) (CA INDEX NAME)



IT 225096-42-4P 225096-43-5P 225096-47-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of substituted aminohydroxyphenylacetamide derivs. as enzyme inhibitors)

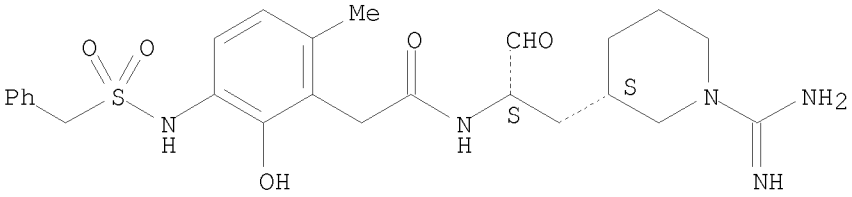
RN 225096-42-4 CAPLUS
CN Benzeneacetamide, N-[(1S)-2-[(3R)-1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-hydroxy-6-methyl-3-[[(phenylmethyl)sulfonyl]amino]- (CA INDEX NAME)

Absolute stereochemistry.

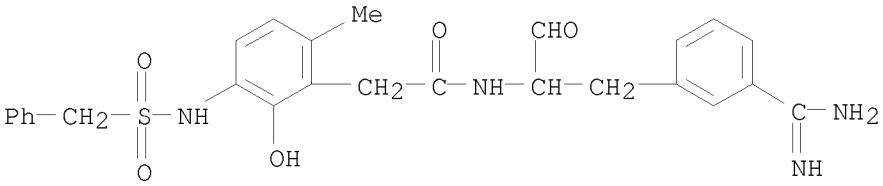


RN 225096-43-5 CAPLUS
CN Benzeneacetamide, N-[(1S)-2-[(3S)-1-(aminoiminomethyl)-3-piperidinyl]-1-formylethyl]-2-hydroxy-6-methyl-3-[[(phenylmethyl)sulfonyl]amino]- (CA INDEX NAME)

Absolute stereochemistry.



RN 225096-47-9 CAPLUS
CN Benzeneacetamide, N-[2-[3-(aminoiminomethyl)phenyl]-1-formylethyl]-2-hydroxy-6-methyl-3-[[(phenylmethyl)sulfonyl]amino]- (CA INDEX NAME)

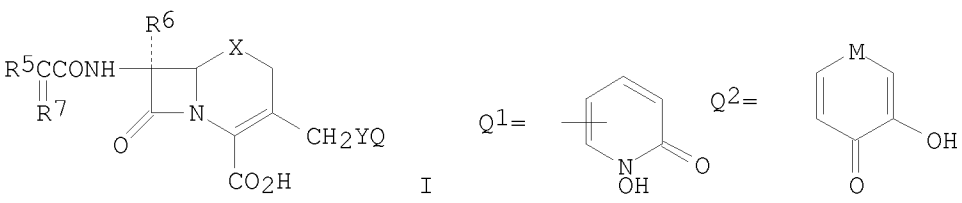


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:154029 CAPLUS
DOCUMENT NUMBER: 110:154029
ORIGINAL REFERENCE NO.: 110:25463a,25466a
TITLE: Preparation of 3-[(aroylamino)methyl]cephalosporins and analogs as antibiotics
INVENTOR(S): Bertrandie, Alain Michel; Jung, Frederic Henri; Bird, Thomas Geoffrey Colerick; Lohmann, Jean Jacques Marcel
PATENT ASSIGNEE(S): ICI Pharma, Fr.
SOURCE: Eur. Pat. Appl., 89 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 267733	A2	19880518	EP 1987-309767	19871104 <--
EP 267733	A3	19891129		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8707987	A	19880831	ZA 1987-7987	19871023 <--
US 5017569	A	19910521	US 1987-117619	19871106 <--
FI 8704939	A	19880513	FI 1987-4939	19871109 <--
AU 8780926	A	19880519	AU 1987-80926	19871109 <--
AU 612990	B2	19910725		
DD 282691	A5	19900919	DD 1987-308889	19871110 <--
DK 8705918	A	19880513	DK 1987-5918	19871111 <--
NO 8704690	A	19880513	NO 1987-4690	19871111 <--
HU 46021	A2	19880928	HU 1987-5010	19871111 <--
HU 202541	B	19910328		
JP 63211288	A	19880902	JP 1987-284415	19871112 <--

PRIORITY APPLN. INFO.: EP 1986-402515 A 19861112
OTHER SOURCE(S): MARPAT 110:154029
GI



I

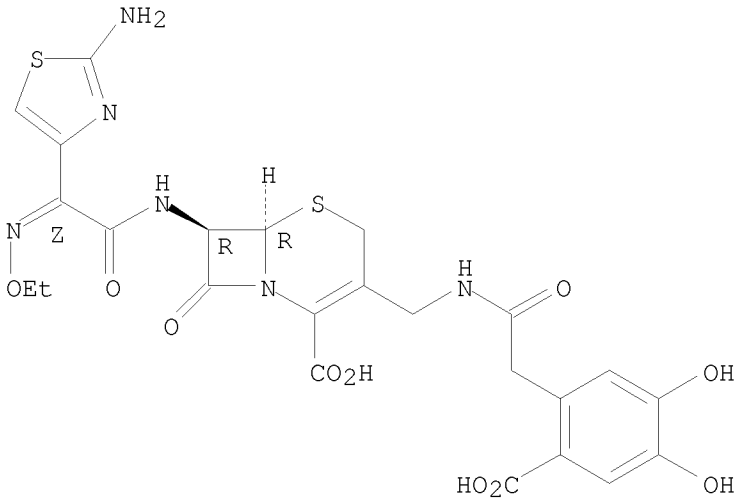
AB The title compds. I [Q = C6H6 ring (optionally fused to a further C6H6 ring to form a naphthyl group, or optionally fused to a heterocyclic aromatic group) with substituents R1 and R2 which are ortho to one another, wherein R1 = OH or an in vivo hydrolyzable ester thereof, and R2 = OH, in vivo hydrolyzable ester thereof, CO2H, SO3H, CH2OH, etc., or Q = Q1, Q2; when Q is a C6H6 ring fused to another C6H6 ring, Q is optionally further substituted by C1-4 alkyl, halo, OH, cyano, etc.; M = O, NR3; R3 = H, C1-4 alkyl; Y = NR4COY1, NR4SO2Y1, etc.; R4 = H, (substituted) C1-4 alkyl, etc.; Y1 = CO, (substituted) C2-4 alkenylene; X = S, O, methylene, sulfinyl; R5 = (substituted) 2-aminothiazol-4-yl, 2-aminooxazol-4-yl, etc.; R6 = H, MeO, NHCHO; R7 = NOR8 (with syn configuration about the double bond); R8 = H, C1-6 alkyl, C3-8 alkyl, C1-3alkyl-C3-6-cycloalkyl, etc.], were prepared as antibiotics. Deacylation of diphenylmethyl 7-(2-thienylacetamido)-3-(3,4-diacetoxybenzoyloxymethyl)ceph-3-em-4-carboxylate gave diphenylmethyl 7-amino-3-(3,4-diacetoxybenzyloxymethyl)ceph-3-em-4-carboxylate (II). Acylation of II with 2-[(Z)-1-(tert-butoxycarbonyl)-1-methylethoxyimino]-2-(2-tritylaminothiazol-4-yl)acetic acid, followed by deprotection, gave 7-[2-(2-aminothiazol-4-yl)-2-(Z)-1-carboxy-1-methylethoxyimino)acetamido]-3-(3,4-dihydroxybenzoyloxymethyl)ceph-3-em-4-carboxylic acid (III). III in vitro exhibited a min. inhibitory concentration of 0.008 μg/mL against Escherichia coli DCO (A8341098).

IT 119733-84-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antibiotic)

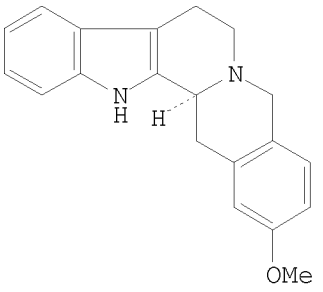
RN 119733-84-5 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl)(ethoxyimino)acetyl]amino]-3-[[[(2-carboxy-4,5-dihydroxyphenyl)acetyl]amino]methyl]-8-oxo-, [6R-[6α,7β(Z)]]- (9CI) (CA INDEX NAME)

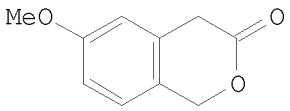
Absolute stereochemistry.
Double bond geometry as shown.



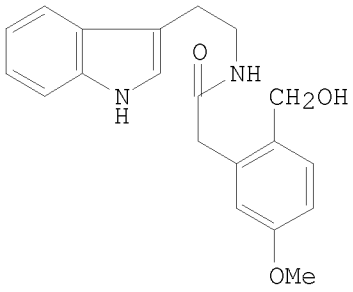
L9 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:221932 CAPLUS
DOCUMENT NUMBER: 108:221932
ORIGINAL REFERENCE NO.: 108:36443a,36446a
TITLE: Synthetic entry into yohimbinoid alkaloids and novel synthesis of (±)-17-methoxyhexadehydroyohimbane
AUTHOR(S): Pandit, Uttam Kumar; Das, Biswanath; Chatterjee, Asima
CORPORATE SOURCE: Dep. Chem., Univ. Coll. Sci., Calcutta, 700 009, India
SOURCE: Tetrahedron (1987), 43(18), 4235-9
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:221932
GI



I

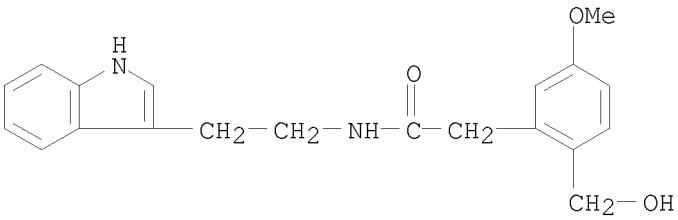


II

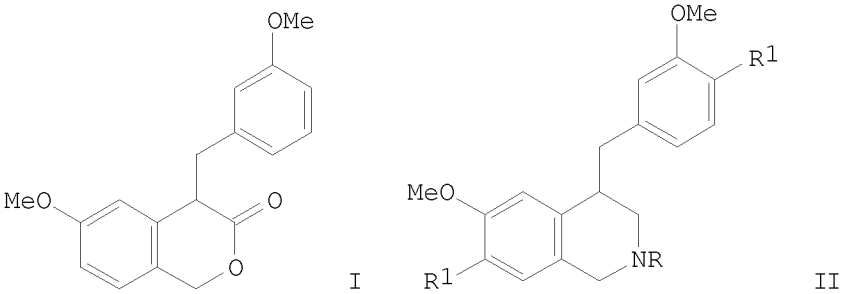


III

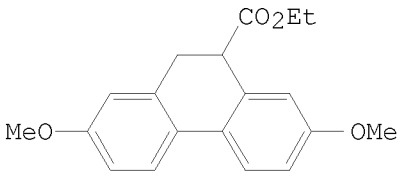
AB The title compound (I) was prepared from m-HOC6H4COMe via condensation of the lactone II with tryptamine and cyclization of the product III by polyphosphate ester.
IT 114547-02-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and intermol. cyclization of, methoxyhexadehydroyohimbane from)
RN 114547-02-3 CAPLUS
CN Benzeneacetamide, 2-(hydroxymethyl)-N-[2-(1H-indol-3-yl)ethyl]-5-methoxy- (CA INDEX NAME)



L9 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1986:148061 CAPLUS
DOCUMENT NUMBER: 104:148061
ORIGINAL REFERENCE NO.: 104:23416h,23417a
TITLE: Electrochemical oxidation of aromatic ethers. Part 10. Regioselectivity in the aryl-aryl coupling reactions of some 4-benzylisochroman-3-ones and benzyl-1,2,3,4-tetrahydroisoquinolines
AUTHOR(S): Majeed, Amera J.; Patel, Premji J.; Sainsbury, Malcolm
CORPORATE SOURCE: Sch. Chem., Univ. Bath, Bath, BA2 7AY, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1985), (6), 1195-9
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 104:148061
GI



I II



III

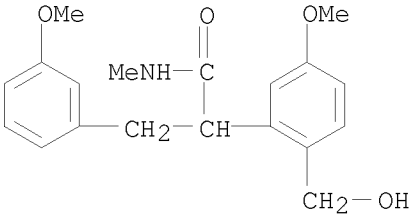
AB The anodic coupling reactions of 4-benzylisochromanone I and 4-benzyl-1,2,3,4-tetrahydroisoquinolines II (R = Me, R1 = H; R= Me, CO2Et, CHO, R1 = OMe) were studied and compared. In neutral media II gave products of coupling to C-1 and/or N-2, depending on the ring substituents. In acid solution, II gave isoaporphines, whereas the 1-benzyl

analogs couple at C-8a to give morphinedienones. The different regioselectivities are due to inductive effects in the protonated bases. I also couples at C-8a but the resulting intermediate is unstable and reacts further with nucleophiles to give 24% 2,5-(OHC)(MeO)C6H3CH(CO2Me)CH2C6H4OMe-3 and 6.3% phenanthrene III.

IT 98748-62-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

RN 98748-62-0 CAPLUS

CN Benzenepropanamide, α-[2-(hydroxymethyl)-5-methoxyphenyl]-3-methoxy-N-methyl- (CA INDEX NAME)



L9 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1969:96552 CAPLUS

DOCUMENT NUMBER: 70:96552

ORIGINAL REFERENCE NO.: 70:18029a,18032a

TITLE: Synthesis of sclerin

AUTHOR(S): Tokoroyama, Takashi; Maeda, S.; Nishikawa, Tomozo; Kubota, Okuo

CORPORATE SOURCE: Osaka City Univ., Osaka, Japan

SOURCE: Tetrahedron (1969), 25(5), 1047-54
CODEN: TETRAB; ISSN: 0040-4020

DOCUMENT TYPE: Journal

LANGUAGE: English

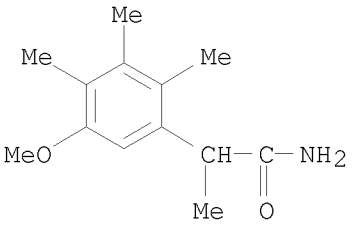
GI For diagram(s), see printed CA Issue.

AB The synthesis of sclerin, which confirms the recently proposed structure I, is described.

IT 13667-26-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 13667-26-0 CAPLUS

CN Hydratropamide, 5-methoxy-2,3,4-trimethyl- (8CI) (CA INDEX NAME)



L9 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1967:94748 CAPLUS
DOCUMENT NUMBER: 66:94748
ORIGINAL REFERENCE NO.: 66:17711a,17714a
TITLE: Synthesis of sclerin and sclerolide, metabolites of Sclerotinia libertiana
AUTHOR(S): Kubota, Takashi; Tokoroyama, Takashi; Nishikawa, Tomozo; Maeda, S.
CORPORATE SOURCE: Univ. Osaka, Osaka, Japan
SOURCE: Tetrahedron Letters (1967), (8), 745-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Hemimellitene (Marinc and Brown, CA 54, 9819f) submitted to Friedel-Crafts acetylation at 20° gave a 5:4 mixture of 2,3,4- and 3,4,5-trimethylacetophenone, separated by fractional distillation over a column.

Nitration of the former isomer gave 68% 2,3,4-trimethyl-5-nitroacetophenone (I, R = NO2) (II), m. 64-6°, along with small amts. of 2,3,4-trimethyl-5,6-dinitroacetophenone, m. 138-40°, and 2,3,4-trimethyl-5-nitrobenzoic acid, m. 176-7°. II was reduced with SnCl2 to the aminoacetophenone I (R = NH2), m. 124-7°, and diazotized to give 53% I (R = OH) (III), m. 168°. III methylated with Me2SO4 and K2CO3 in Me2CO followed by reduction with LiAlH4 gave 1-(1-hydroxyethyl)-5-methoxy-2,3,4-trimethylbenzene (IV), m. 68-9°, identical with a specimen from sclerin (V). IV treated with SOCl2, the chloride heated with NaCN in Me2SO at 120°, and the nitrile heated with aqueous 20% KOH and HOCH2CH2OH gave the nor-acid methyl ether (VI, R = H, R' = Me) (VII), m. 131° (amide m. 126-8°), obtained by milder hydrolysis. Demethylation of VII with HI gave the nor-acid VI (R = R' = H) (VIII), m. 128-30°. The identity of VII and VIII with the corresponding compds. from V was shown by ir spectral comparison. VII nitrated in Ac2O at -30° gave the nitro acid (IX, R = NO2), m. 208-9°, reduced catalytically in warm AcOH in the presence of Pd-C to give the 5-membered lactam (X), m. 211-13°, unsuitable for further transformation by the Sandmeyer reaction. VI (R = R' = Me) was chloromethylated and with concomitant lactonization gave 76% 6-membered lactone (XI), m. 115-16°. XI oxidized 24 hrs. with Jones reagent gave 30% IX (R = CO2H), converted by hot Ac2O to sclerin methyl ether (XII), m. 104-5°, demethylated with BBr3 to racemic V. III nitrated in a mixture of AcOH and CCl4 yielded 80% 3-hydroxy-4,5,6-trimethyl-2-nitroacetophenone (XIII, R = NO2, R' = H), m. 99-100°, converted to the Na salt and methylated with Me2SO4 in refluxing C6H6 to the 3-methoxy derivative XIII (R = NO2, R' = Me), m. 70-2°. Further transformation by treatment with SnCl2 gave the amine XIII (R = NH2, R' = Me) (XIV), when as insufficient reduction led to formation of 7-methoxy-3,4,5,6-tetramethylanthranil, m. 80°. Conversion of XIV by the Sandmeyer reaction gave XIII (R = CN, R' = Me), hydrolyzed in alkali to yield sclerolide Me ether (XV, R = Me), m. 145.5-6.5°, demethylated with HBr to sclerolide XV (R = H), identical with the natural product from S. libertiana.

IT 13667-26-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 13667-26-0 CAPLUS
CN Hydratropamide, 5-methoxy-2,3,4-trimethyl- (8CI) (CA INDEX NAME)